STIC Search Report
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STIC Database Tracking Number: 130896

TO: Zohreh Fay **Location: 3a61 / 3c70** **Wednesday, September 01, 2004** **Art Unit: 1614** **Phone: 272-0573** **Serial Number: 10 / 659708**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

1 50 696

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Zohreh Fay Examiner #: 66646 Date: 8/26/04

Art Unit: 1614 Phone Number 571-272-0573 Serial Number: 10/659,708

Mail Box and Bldg/Room Location: 3C70/3461 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: # Methods for treating lung cancer using insulin-like growth factor.

Inventors (please provide full names): _____

Earliest Priority Filing Date: 9/11/02

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

please search the claimed method of use.

Jan

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#)	STN ✓
Searcher Phone #: 22504	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 9/1	Bibliographic ✓	Dr.Link
Date Completed: 9/1	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 10	Patent Family	WWW/Internet
Online Time: +25	Other	Other (specify)

PTO-1590 (8-01)

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:02:44 ON 01 SEP 2004
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FILE COVERS 1907 - 1 Sep 2004  VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004  (20040831/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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     (FILE 'HOME' ENTERED AT 11:46:07 ON 01 SEP 2004)
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     FILE 'HCAPLUS' ENTERED AT 11:46:16 ON 01 SEP 2004
               E IGFBP
L1          859 S E12-E15
L2         2926 S E3()3
L3         1267 S INSULIN LIKE GROWTH FACTOR BINDING PROTEIN 3
L4         3278 S L1-L3
               E INSULIN/CT
L5         2241 S E70,E76
               E E62+ALL
L6         1156 S E2
L7         3532 S L4-L6
               E LUNG NEOPLASM/CT
L8        24960 S E53-E69
               E E53+ALL
L9        25811 S E21,E20+NT
L10          62 S L7 AND L8,L9
L11           1 S US20040127411/PN OR (WO2003-US28354 OR US2002-409852#)/AP,PRN
               E INSMED/PA,CS
L12          17 S E3-E26
               E LEYLAND JONES/AU
L13          86 S E4-E6
               E LEYLAND B/AU
L14           1 S L10 AND L11-L13
L15          50 S L10 AND (PD<=20020911 OR PRD<=20020911 OR PD<=20020911)
L16          13 S L15 AND (PHARMACEUT? OR PHARMACOL? OR IMMUN?)/SC,SX
L17          12 S L16 NOT L14
               SEL DN AN 4 6 10
L18           9 S L17 NOT E1-E9
L19          10 S L14,L18
L20          37 S L15 NOT L16-L19
               SEL DN AN L20 2 4 5 9 11 18 20-22 24 28 30
L21          12 S E10-E45 AND L20
L22          22 S L19,L21
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L23          12 S L10 NOT L15-L22
                SEL DN AN L23 10
L24           1 S E46-E48 AND L23
L25          23 S L22,L24
L26          23 S L25 AND (IGF OR IGFBP OR BINDING PROTEIN)

     FILE 'HCAPLUS' ENTERED AT 12:02:44 ON 01 SEP 2004

=> d all tot l26

L26  ANSWER 1 OF 23  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:252365  HCAPLUS
DN   140:247046
ED   Entered STN:  26 Mar 2004
TI   Methods for treating cancer, particularly lung cancer, using
     insulin-like growth factor
     binding protein-3
IN   Leyland-jones, Brian
PA   Insmed, Inc., USA
SO   PCT Int. Appl., 29 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K038-28
CC   1-6 (Pharmacology)
     Section cross-reference(s): 2
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    --------------------   --------
PI   WO 2004024179        A1    20040325    WO 2003-US28354        20030911 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
     US 2004127411         A1    20040701    US 2003-659708         20030911 <--
PRAI US 2002-409852P       P     20020911  <--
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------   -----  ----------------------------------------------
 WO 2004024179    ICM    A61K038-28
AB   The invention discloses the use of insulin like
     growth factor binding protein-
     3 (IGFBP-3) as an antineoplastic agent.  More
     particularly, the invention discloses the use of IGFBP-3
     in the treatment of patients with lung cancer.
ST   cancer treatment insulin like growth
     factor binding protein 3; lung
     cancer antitumor IGFBP3
IT   Insulin-like growth factor-binding proteins
     RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (IGFBP-3; insulin-like
        growth factor binding protein-
        3 for treating cancer, particularly lung cancer)
IT   Drug resistance
        (antitumor; insulin-like growth
```

factor binding protein-3 for
treating cancer, particularly lung cancer)
IT Intestine, neoplasm
(colorectal carcinoma; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT Drug delivery systems
(infusions, i.v.; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT Drug delivery systems
(injections, i.v.; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT Drug delivery systems
(injections, s.c.; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT Antitumor agents
Drug delivery systems
Drug interactions
Human
Lung, neoplasm
Mammary gland, neoplasm
Radiosensitizers, biological
Radiotherapy
(**insulin-like growth factor binding protein-3** for treating cancer,
particularly lung cancer)
IT neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**insulin-like growth factor binding protein-3** for treating cancer,
particularly lung cancer)
IT Drug delivery systems
(parenterals; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT Antitumor agents
(resistance to; **insulin-like growth factor binding protein-3** for
treating cancer, particularly lung cancer)
IT 41575-94-4, Carboplatin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**insulin-like growth factor binding protein-3** for treating cancer,
particularly lung cancer)
IT 33069-62-4, Paclitaxel 97682-44-5, Irinotecan 180288-69-1, Herceptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(**insulin-like growth factor binding protein-3** for treating cancer,
particularly lung cancer)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) West, S; US 5681818 1997 HCAPLUS

L26 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80714 HCAPLUS
DN 140:141434
ED Entered STN: 01 Feb 2004
TI Human protein sequences of protein complexes of cellular networks
underlying the development of cancer and other diseases

IN Merino, Alejandro; Bouwmeester, Tewis; Bauer, Andreas; Drewes, Gerard; Marzioch, Martina; Kruse, Ulrich; Superti-Furga, Giulio; Eberhard, Dirk; Ruffner, Heinz; Hobson, Scott; Helftenbein, Gerd; Cruciat, Cristina
PA Cellzome Ag, Germany; et al.
SO PCT Int. Appl., 810 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-39
CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 14
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004009622	A2	20040129	WO 2003-EP7835	20030718 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	EP 2002-16109	A	20020719 <--
	EP 2002-16111	A	20020719 <--
	EP 2002-16123	A	20020719 <--
	EP 2002-16128	A	20020719 <--
	EP 2002-16427	A	20020722 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004009622	ICM	C07K014-39

AB The present invention relates to protein complexes involved in cellular processes which have been shown to be critical for the development of various forms of cancer, component proteins of the said complexes, fragments and derivs. of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

ST human protein complex sequence cancer diagnosis drug therapy

IT Cyclins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, complexes; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Transport proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ABC (ATP-binding cassette) transporters, family D-member 3; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Transport proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ABCC3 (ATP-binding cassette transporter sub-family C member 3); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Transport proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ADP/ATP carrier; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ARP2 (actin-related protein 2); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAG-1 (Bcl2-associated athanogene 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BIK (Bcl-2-interacting killer); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BNIP3; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BTG1; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bad; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bax; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bcl-2; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bim; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CAF-1 (chromatin assembly factor I), subunit C; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CBL; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins

RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CDC37; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Antigens
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CENP-F (centromere-associated protein F); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Enzymes, biological studies
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA helicase II; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-binding, UV-damaged; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Gene, animal
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ERBIN; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GAB1 (GRB2-associated binder 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GRB (growth factor receptor-bound), GRB7; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GRB-2 (growth factor receptor-bound protein 2); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Cell migration
(Gab1 signaling protein complex; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Epidermal growth factor receptors
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HER4; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Heat-shock proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HSP 90, α; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT **Insulin-like growth factor-binding proteins**
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**IGFBP-3**; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRS-1 (insulin receptor substrate 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IRS-2 (insulin receptor substrate 2); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAD2 (mitotic arrest deficient 2), MAD2L1; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT DNA formation factors
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MCM4; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MLH3; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MSH6; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Antigens
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NY-CO-7; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDCD (programmed cell death), 2; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RAD50; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RAP1 (repressor/activator site-**binding protein** 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RINGO1; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Enzymes, biological studies
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RNA helicase; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT GTPase-activating protein
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RasGAP; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SHC; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SKP1 (S-phase kinase-associated protein 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRF1 (telomeric repeat-binding factor 1); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TRF2 (telomere repeat-binding factor 2); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Ribonucleoproteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(U5 snRNP (U5 snRNA-containing small nuclear ribonucleoprotein); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Anion channel
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VDAC (voltage-dependent anion channel); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Annexins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VI; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WD repeat-containing; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Glycoproteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ZAG (zinc-α2-glycoprotein); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Purification

(affinity; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Transport proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid transporter, excitatory; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Nervous system, disease
(amyotrophic lateral sclerosis; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-Raf; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-crk; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Intestine, neoplasm
(colon; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Intestine, neoplasm
(colorectal; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(complexes; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complexes; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Nervous system, disease
(degeneration; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Interleukins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancer binding factor 3; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Growth factor receptors
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erbB-3, HER$; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Agglutinins and Lectins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(galectin-7; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins

RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene CDC2, complexes; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Phosphoproteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene cdk2, complexes; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Ribonucleoproteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hnRNP (heterogeneous nuclear ribonucleoprotein); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Ribonucleoproteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hnRNP H2 (heterogeneous nuclear ribonucleoprotein H2); human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Alzheimer's disease
Bladder, neoplasm
Buffers
Chemotherapy
Disease, animal
Drug design
Drug screening
Drugs
Genetic vectors
Human
Labels
Leukemia
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Melanoma
Microarray technology
Molecular cloning
Multiple myeloma
Neoplasm
Nucleic acid hybridization
Ovary, neoplasm
Prognosis
Prostate gland, neoplasm
Protein sequences
Psoriasis
Stomach, neoplasm
Susceptibility (genetic)
Test kits
Transcriptional regulation
Transformation, genetic
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Reagents
RL: ARG (Analytical reagent use); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Nucleic acids
RL: DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES

(Uses)
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Actins
Epidermal growth factor receptors
Filamin
GTPase-activating protein
Glial fibrillary acidic protein
Hepatocyte growth factor receptors
Proliferating cell nuclear antigen
Transcription factors
Transferrin receptors
neu (receptor)
neu (receptor)
α1-Acid glycoprotein
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Antibodies and Immunoglobulins
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Apoptosis
(induction, by Bcl-2; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Neoplasm
(metastasis, by Gab1 protein complex; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Diagnosis
(mol.; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutS; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nuclear matrix-associated; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleolar organizer-associated; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleophosmin; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleoplasmins; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other

diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p120; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p23; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Ras proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p23R-ras; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p30; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Animal tissue
Cell
Organ, animal
(protein expression in; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant, protein fused with tag or label; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(semaphorin 3A; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Neoplasm
(solid; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(telokins; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Transport proteins
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tricarboxylate transporter; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT Amyloid
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)
IT 652207-39-1, Protein (human) 652208-91-8, Protein (human) 652208-92-9, Protein (human) 652208-93-0, Protein (human) 652208-94-1, Protein (human) 652208-95-2, Protein (human) 652208-96-3, Protein (human) 652208-97-4, Protein (human) 652208-98-5, Protein (human) 652208-99-6, Protein (human) 652209-00-2, Protein (human) 652209-01-3, Protein

(human) 652209-02-4, Protein (human) 652209-03-5, Protein (human) 652209-04-6, Protein (human) 652209-05-7, Protein (human) 652209-06-8, Protein (human) 652209-07-9, Protein (human) 652209-08-0, Protein (human) 652209-09-1, Protein (human) 652209-10-4, Protein (human) 652209-11-5, Protein (human) 652209-12-6, Protein (human) 652209-13-7, Protein (human) 652209-14-8, Protein (human) 652209-15-9, Protein (human) 652209-16-0, Protein (human) 652209-17-1, Protein (human) 652209-18-2, Protein (human) 652209-19-3, Protein (human) 652209-20-6, Protein (human) 652209-21-7, Protein (human) 652209-22-8, Protein (human) 652209-23-9, Protein (human) 652209-24-0, Protein (human) 652209-25-1, Protein (human) 652209-26-2, Protein (human) 652209-27-3, Protein (human) 652209-28-4, Protein (human) 652209-29-5, Protein (human) 652209-30-8, Protein (human) 652209-31-9, Protein (human) 652209-32-0, Protein (human) 652209-33-1, Protein (human) 652209-34-2, Protein (human) 652209-35-3, Protein (human) 652209-36-4, Protein (human) 652209-37-5, Protein (human) 652209-38-6, Protein (human) 652209-39-7, Protein (human) 652209-40-0, Protein (human) 652209-41-1, Protein (human) 652209-42-2, Protein (human) 652209-43-3, Protein (human) 652209-44-4, Protein (human) 652209-45-5, Protein (human) 652209-46-6, Protein (human) 652209-47-7, Protein (human) 652209-48-8, Protein (human) 652209-49-9, Protein (human) 652209-50-2, Protein (human) 652209-51-3, Protein (human) 652209-52-4, Protein (human) 652209-53-5, Protein (human) 652209-54-6, Protein (human) 652209-55-7, Protein (human) 652209-56-8, Protein (human) 652209-57-9, Protein (human) 652209-58-0, Protein (human) 652209-59-1, Protein (human) 652209-60-4, Protein (human) 652209-61-5, Protein (human) 652209-62-6, Protein (human) 652209-63-7, Protein (human) 652209-64-8, Protein (human) 652209-65-9, Protein (human) 652209-66-0, Protein (human) 652209-67-1, Protein (human) 652209-68-2, Protein (human) 652209-69-3, Protein (human) 652209-70-6, Protein (human) 652209-71-7, Protein (human) 652209-72-8, Protein (human) 652209-73-9, Protein (human) 652209-74-0, Protein (human) 652209-75-1, Protein (human) 652209-76-2, Protein (human) 652209-77-3, Protein (human) 652209-78-4, Protein (human) 652209-79-5, Protein (human) 652209-80-8, Protein (human) 652209-81-9, Protein (human) 652209-82-0, Protein (human) 652209-83-1, Protein (human) 652209-84-2, Protein (human) 652209-85-3, Protein (human) 652209-86-4, Protein (human) 652209-87-5, Protein (human) 652209-88-6, Protein (human) 652209-89-7, Protein (human) 652209-90-0, Protein (human) 652209-91-1, Protein (human) 652209-92-2, Protein (human) 652209-93-3, Protein (human) 652209-94-4, Protein (human) 652209-95-5, Protein (human) 652209-96-6, Protein (human) 652209-97-7, Protein (human) 652209-98-8, Protein (human) 652209-99-9, Protein (human) 652210-00-9, Protein (human) 652210-01-0, Protein (human) 652210-02-1, Protein (human) 652210-03-2, Protein (human) 652210-04-3, Protein (human) 652210-05-4, Protein (human) 652210-06-5, Protein (human) 652210-07-6, Protein (human) 652210-08-7, Protein (human) 652210-09-8, Protein (human) 652210-10-1, Protein (human) 652210-11-2, Protein (human) 652210-12-3, Protein (human) 652210-13-4, Protein (human) 652210-14-5, Protein (human) 652210-15-6, Protein (human) 652210-16-7, Protein (human) 652210-17-8, Protein (human) 652210-18-9, Protein (human) 652210-19-0, Protein (human) 652210-20-3, Protein (human) 652210-21-4, Protein (human) 652210-22-5, Protein (human) 652210-23-6, Protein (human) 652210-24-7, Protein (human) 652210-25-8, Protein (human) 652210-26-9, Protein (human) 652210-27-0, Protein (human) 652210-28-1, Protein (human) 652210-29-2, Protein (human) 652210-30-5, Protein (human) 652210-31-6, Protein (human) 652210-32-7, Protein (human) 652210-33-8, Protein (human) 652210-34-9, Protein (human) 652210-35-0, Protein (human) 652210-36-1, Protein (human) 652210-37-2, Protein (human) 652210-38-3, Protein (human) 652210-39-4 652210-40-7, Protein (human) 652210-41-8, Protein (human) 652210-42-9, Protein (human) 652210-43-0, Protein (human) 652210-44-1, Protein (human) 652210-45-2, Protein (human) 652210-46-3, Protein (human) 652210-47-4, Protein (human) 652210-48-5, Protein (human) 652210-49-6,

Protein (human) 652210-50-9, Protein (human) 652210-51-0, Protein (human) 652210-52-1, Protein (human) 652210-53-2, Protein (human) 652210-54-3, Protein (human) 652210-55-4, Protein (human) 652210-56-5, Protein (human) 652210-57-6, Protein (human) 652210-58-7, Protein (human) 652210-59-8, Protein (human) 652210-60-1, Protein (human) 652210-61-2, Protein (human) 652210-62-3, Protein (human) 652210-63-4, Protein (human) 652210-64-5, Protein (human) 652210-65-6, Protein (human) 652210-66-7, Protein (human) 652210-67-8, Protein (human) 652210-68-9, Protein (human) 652210-69-0, Protein (human) 652210-70-3, Protein (human) 652210-71-4, Protein (human) 652210-72-5, Protein (human) 652210-73-6, Protein (human) 652210-74-7, Protein (human) 652210-75-8, Protein (human) 652210-76-9, Protein (human) 652210-77-0, Protein (human) 652210-78-1, Protein (human) 652210-79-2, Protein (human) 652210-80-5, Protein (human) 652210-81-6, Protein (human) 652210-82-7, Protein (human)
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT 9023-70-5, Glutamine synthetase 9027-01-4 9028-06-2, Proline 4 hydroxylase 9030-23-3, Thymidine phosphorylase 9030-74-4, Dihydropyrimidinase 9047-64-7, Ribonucleoside diphosphate reductase 9054-51-7, Histone acetyl transferase 37318-49-3 50864-48-7, Sphingosine kinase 60382-71-0, Diacylglycerol kinase 80449-01-0, DNA topoisomerase 86480-67-3, Ubiquitin carboxyl terminal hydrolase 115926-52-8, PI3-kinase 116283-83-1, Elongation factor 2 kinase 119699-77-3, Inositol polyphosphate 5-phosphatase 137632-09-8, HER2 Kinase 140879-24-9, Proteasome 148938-24-3, Meprin A 150605-49-5, Palmitoyl protein thioesterase 1 192140-82-2, Squamous cell carcinoma antigen 1 205944-60-1, Squamous cell carcinoma antigen 2 213390-44-4, ATP-dependent metalloprotease 303752-61-6, DNA-dependent protein kinase 362479-32-1, Serine threonine protein phosphatase 1 362674-81-5 372092-80-3, Protein kinase
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT 9014-24-8, DNA-dependent RNA polymerase
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoform II; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT 9004-06-2, Elastase
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of leukocytes, of leukocytes, inhibitor; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT 9001-92-7, Protease
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tags separated by cleavage site for a; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

IT 366806-33-9, Casein kinase II
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α chain; human protein sequences of protein complexes of cellular networks underlying the development of cancer and other diseases)

L26 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:18721 HCAPLUS
DN 140:71004
ED Entered STN: 09 Jan 2004
TI Viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer
IN Lee, Ho-young
PA USA
SO U.S. Pat. Appl. Publ., 82 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K048-00
ICS A61K038-18
NCL 424093200; 514002000; 514044000
CC 1-6 (**Pharmacology**)
Section cross-reference(s): **15, 63**

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004005294	A1	20040108	US 2003-377142	20030225 <--
PRAI US 2002-359536P	P	20020225 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004005294	ICM	A61K048-00
	ICS	A61K038-18
	NCL	424093200; 514002000; 514044000

AB The present invention provides methods of inhibiting cancer cell growth by using insulin-like growth factor-**binding protein IGFBP-3** polypeptides and expression constructs coding therefor. In a particular aspect, the invention provides adenoviral constructs expressing **IGFBP-3**, and their use to inhibit non-small cell lung cancer. In addition, **IGFBP-3** expression can be diagnostic of cancer development and progression. Methods for assessing **IGFBP-3** expression, for example using promoter methylation assays, are described.

ST viral vector **IGFBP3** diagnosis antitumor lung cancer

IT Genetic methods
(DNAse protection, for detecting **IGFBP-3** gene mutation; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E1, deletion of; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

IT **Insulin-like growth factor-binding proteins**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**IGFBP-3**; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

IT Estrogen receptors
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding agent, for cancer therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cancer tissue-specific, inducible, constitutive; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

IT Intestine, neoplasm
(colon; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Adenoviral vectors
Genetic vectors
Retroviral vectors
(encoding **IGFBP-3**; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT DNA sequence analysis
RFLP (restriction fragment length polymorphism)
(for detecting **IGFBP-3** gene mutation; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Neoplasm
(hematol.; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(immediate early, CMV; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Drug delivery systems
(intratumoral, systemic; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Microwave
UV radiation
(irradiation, therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Gamma ray
(irradiation; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT PCR (polymerase chain reaction)
(methylation specific; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Neck, anatomical
(neoplasm; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT **Lung, neoplasm**
(**non-small-cell carcinoma**, treatment of; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(non-viral vector encapsulated with; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Mutation
(of **IGFBP-3** gene; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Methylation
(of the **IGFBP-3** promoter; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene, antisense, therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide, therapy; viral vectors encoding **IGFBP-3**

and use for the diagnosis and treatment of cancer)
IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyadenylation signal, **IGFBP-3** encoding vector comprising; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pro-apoptotic, therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Cytomegalovirus
(promoter; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single chain, anti-oncogene, therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Antibodies and Immunoglobulins
Cytokines
Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Adeno-associated virus
Herpesviridae
Papillomavirus
Vaccinia virus
(vector, encoding **IGFBP-3**; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Antitumor agents
Brain, neoplasm
Chemotherapy
Esophagus, neoplasm
Gene therapy
Head, neoplasm
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Radiotherapy
Skin, neoplasm
Stomach, neoplasm
Surgery
Testis, neoplasm
Uterus, neoplasm
(viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT Radiotherapy
(x-ray; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT 50-07-7, Mitomycin 50-18-0, Cyclophosphamide 50-76-0, Dactinomycin
51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 55-98-1, Busulfan
57-22-7, Vincristin 59-05-2, Methotrexate 148-82-3, Melphalan
305-03-3, Chlorambucil 671-16-9, Procarbazine 865-21-4, Vinblastin
3778-73-2, Ifosfamide 7689-03-4, Camptothecin 10540-29-1, Tamoxifen
11056-06-7, Bleomycin 13010-20-3, Nitrosurea 14913-33-8 15663-27-1,
Cisplatin 18378-89-7, Plicamycin 20830-81-3, Daunorubicin
23214-92-8, Doxorubicin 33069-62-4, Taxol 33419-42-0, Etoposide
41575-94-4, Carboplatin 84449-90-1, Raloxifene 95058-81-4, Gemcitabine

125317-39-7, Navelbine
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for cancer therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)
IT 131384-38-8, Protein farnesyl transferase
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, for cancer therapy; viral vectors encoding **IGFBP-3** and use for the diagnosis and treatment of cancer)

L26 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:950024 HCAPLUS
DN 140:13080
ED Entered STN: 05 Dec 2003
TI **IGF-binding protein**-derived peptide or small molecule
IN Mascarenhas, Desmond
PA USA
SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 264,672.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-00
NCL 514012000
CC 1-12 (**Pharmacology**)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003224990	A1	20031204	US 2003-383999	20030307 <--
	US 2003059430	A1	20030327	US 2002-215759	20020809 <--
	US 2003161829	A1	20030828	US 2002-264672	20021004 <--
PRAI	US 2001-323267P	P	20010918 <--		
	US 2002-215759	A2	20020809 <--		
	US 2002-264672	A2	20021004		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003224990	ICM	A61K038-00
	NCL	514012000
US 2003224990	ECLA	A61K038/30 <--
US 2003161829	ECLA	A61K038/30 <--

AB New compns. based on **IGF-binding protein** sequences are provided. The peptides of the invention have the following biol. property pro-apoptotic, antiangiogenic, antiinflammatory, cardiovascular, metal-binding, ECM-binding, cell internalization, protease inhibition, transcriptional modulation, cell imaging, and expression tag properties. New tools for high-throughput research are provided. New methods for the treatment of human disease are provided. **IGFBP-3**-derived peptide or small mol. is administered to subjects having disease, thereby alleviating the symptoms of the disease. The diseases that can be treated include cancer, autoimmune disease, cardiovascular indications, arthritis, asthma and allergy, reproductive indications, retinal proliferative disease, bone disease, inflammatory disease, inflammatory bowel disease, and fibrotic disease.
ST **IGFBP** peptide therapeutic use
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Bax, expression of Bax-α is stimulated by IFGBP3 and peptides; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Extracellular matrix
(ECM-binding activity; **IGF-binding protein**

-derived peptide or small mol. with therapeutic properties)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IAP (integrin-associated protein), proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent;
IGF-binding protein-derived peptide or
small mol. with therapeutic properties)
IT Allergy
Allergy inhibitors
Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antitumor agents
Arthritis
Asthma
Autoimmune disease
Bone, disease
Cardiovascular agents
Chelating agents
Fibrosis
Human
Imaging agents
Immunomodulators
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Peptidomimetics
Prostate gland, neoplasm
Stomach, neoplasm
(**IGF-binding protein**-derived peptide or
small mol. with therapeutic properties)
IT Insulin-like growth factor-**binding proteins**
Peptides, biological studies
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF-binding protein**-derived peptide or
small mol. with therapeutic properties)
IT **Insulin-like growth factor-binding proteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3**; **IGF-binding**
protein-derived peptide or small mol. with therapeutic
properties)
IT Mammary gland, neoplasm
(adenocarcinoma; **IGF-binding protein**
-derived peptide or small mol. with therapeutic properties)
IT Signal transduction, biological
(apoptotic activity of **IGFBP** peptides is dependent on
PI3K/ILK signal transduction; **IGF-binding**
protein-derived peptide or small mol. with therapeutic
properties)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(caveolins, **IGFBP** derived peptide contains a caveolin
consensus binding site; **IGF-binding protein**
-derived peptide or small mol. with therapeutic properties)
IT Biological transport
(cell internalization activity; **IGF-binding**
protein-derived peptide or small mol. with therapeutic
properties)

IT Intestine, neoplasm
(colon; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Reproduction, animal
(disorder; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression tag properties; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Intestine, disease
(inflammatory; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Biological transport
(intracellular, nuclear translocation of **IGFBP** peptides involves caveolin- and; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Transcription, genetic
(modulators; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Cell nucleus
(nuclear translocation of **IGFBP** peptides involves caveolin- and clathrin-mediated pathways; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Endocytosis
(nuclear translocation of **IGFBP** peptides involves caveolin- and; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Transferrin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Apoptosis
(proapototic activity; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Eye, disease
(retinopathy, retinal proliferative disease; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αv, proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α5, proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α6, proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(β5, proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1, proapoptotic and cell internalization activities of **IGFBP** peptides are integrin dependent; **IGF-binding protein**-derived peptide or small mol. with therapeutic properties)

IT 630155-72-5 630155-73-6 630155-74-7 630155-75-8 630155-76-9
630155-77-0 630155-78-1 630155-79-2 630155-80-5 630155-81-6
RL: PRP (Properties)
(unclaimed sequence; **iGF-binding protein**-derived peptide or small mol.)

L26 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:656520 HCAPLUS
DN 139:159924
ED Entered STN: 22 Aug 2003
TI Use of **insulin-like growth factor binding protein 3** (**IGF**-BP3) for inhibition of tumor growth
IN Kirman, Irena; Whelan, Richard
PA The Trustees of Columbia University, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-6 (**Pharmacology**)
Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068160	A2	20030821	WO 2003-US4315	20030213 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004048794	A1	20040311	US 2003-366881	20030213 <--
PRAI	US 2002-357000P	P	20020213 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003068160	ICM	A61K

AB A method of inhibiting proliferation of cells associated with a tumor in a subject comprises administering to the subject a tumor cell proliferation-inhibiting amount of **IGF**-BP3, thereby inhibiting proliferation of the cells. An improved surgical method comprises surgically resecting a tumor from a subject and administering to the subject an amount of a protein effective to inhibit metastasis of any tumor cells released in the subject's blood circulation during the surgical resection of the tumor.

ST surgery tumor **IGFBP3**; antitumor **insulin like growth factor binding protein**

3
IT **Insulin-like growth factor-binding proteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3; insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Intestine, neoplasm
(colon, adenocarcinoma; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Intestine, neoplasm
(colon, adenoma; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Intestine
(colon, colorectomy; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Intestine, neoplasm
(colon; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Intestine, neoplasm
(colorectal; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Stomach
(gastric bypass surgery; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Drug delivery systems
(injections, i.v.; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Antitumor agents
Drug delivery systems
Human
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
Prostate gland, neoplasm
Surgery
(**insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Neoplasm
(metastasis; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Surgery
(open abdominal surgery; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Drug delivery systems
(oral; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)
IT Drug delivery systems
(transdermal; **insulin-like growth factor binding protein 3** for inhibition of tumor growth)

L26 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2003:491391** HCAPLUS
DN **139:31260**
ED Entered STN: 27 Jun 2003
TI Mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for the treatment of cancers
IN Rechler, Mathew M.
PA Department of Health and Human Services, USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 2-6 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003052079	A2	20030626	WO 2002-US40561	20021217 <--
	WO 2003052079	A3	20031127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-341920P P 20011217 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003052079	ICM	C12N

AB An isolated or purified nucleic acid mol. consisting essentially of a nucleotide sequence encoding a mutant human **IGFBP-3**, which can inhibit DNA synthesis, can induce apoptosis, binds to neither human insulin growth factor-I (**IGF**-I), nor human insulin growth factor-II (**IGF**-II), and comprises a mutation at Y57; a vector comprising the same, a cell comprising and expressing the same, optionally in the form of a vector; an isolated or purified polypeptide mol. consisting essentially of an amino acid sequence encoding a mutant human **IGFBP-3**, which can inhibit DNA synthesis, can induce apoptosis, binds to neither human **IGF**-I nor human **IGF**-II and comprises a mutation at Y57; a composition comprising the same; and a method of inducing apoptosis in a cell, which method comprises administering to the cell the nucleic acid mol. or polypeptide mol., in an amount sufficient to induce apoptosis in the cell, whereupon apoptosis is induced in the cell.
ST **IGFBP3** mutant apoptosis human cancer treatment
IT Protein motifs
(**IGF**-binding domain of **IGFBP3**, mutated; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT **Insulin-like growth factor-binding proteins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3**, mutants; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for

treatment of cancers)
IT Apoptosis
(**IGFBP3** mutant-induced; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT DNA formation
(**IGFBP3** mutant-inhibited; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT Leukemia
(childhood-onset; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT Intestine, neoplasm
(colorectal; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT Human
Lung, neoplasm
Neoplasm
Prostate gland, neoplasm
(mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT Mutagenesis
(site-directed, substitution; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT 74-79-3, Arginine, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGFBP3** Arg75 mutant; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT 73-32-5, Isoleucine, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGFBP3** Ile56 mutant; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT 61-90-5, Leucine, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGFBP3** Leu77, Leu80 and Leu81 mutant; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT 60-18-4, Tyrosine, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGFBP3** Tyr57 mutant; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)
IT 67763-96-6, **IGF**-I 67763-97-7, **IGF**-II
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(not binding to **IGFBP3** mutant; mutants of human **insulin-like growth factor binding protein-3** (**IGFBP-3**) and uses for treatment of cancers)

L26 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2003:411507** HCAPLUS
DN **139:177584**
ED Entered STN: 30 May 2003
TI The insulin-like growth factor system and cancer
AU LeRoith, Derek; Roberts, Charles T.
CS National Institutes of Health MSC 1758, Bethesda, MD, 20892-1758, USA
SO Cancer Letters (Oxford, United Kingdom) (2003), 195(2), 127-137
CODEN: CALEDQ; ISSN: 0304-3835
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB A review. The insulin-like growth factor (**IGF**) family of ligands, **binding proteins** and receptors is an important growth factor system involved in both the development of the organism and the maintenance of normal function of many cells of the body. The system also has powerful anti-apoptotic effects. More recently, evidence has accrued to demonstrate that the **IGFs** play an important role in cancer. Individuals with serum **IGF**-II levels in the upper quartile of the normal range (and **IGF binding protein**-3 levels in the lower quartiles) have a relative risk for developing breast, prostate, colon and lung cancer. **IGF**-II is commonly expressed by tumor cells and may act as an autocrine growth factor; occasionally even reaching target tissues and causing tumor-induced hypoglycemia. The **IGF**-I receptor is commonly (though not always) overexpressed in many cancers, and many recent studies have identified new signaling pathways emanating from the **IGF**-I receptor that affect cancer cell proliferation, adhesion, migration and cell death; functions that are critical for cancer cell survival and metastases. In this review, many aspects of the **IGF** system and its relationship to cancer will be discussed.
ST review **IGF** receptor **IGFBP** cancer
IT Adhesion, biological
Cell migration
Cell proliferation
Human
Hypoglycemia
Lung, neoplasm
Mammary gland, neoplasm
Prostate gland, neoplasm
Signal transduction, biological
(**IGF** system and cancer)
IT Insulin-like growth factor I receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF** system and cancer)
IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGFBP-3**; **IGF** system and cancer)
IT Intestine, neoplasm
(colon; **IGF** system and cancer)
IT Neoplasm
(metastasis; **IGF** system and cancer)
IT 67763-97-7, **IGF**-II
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF** system and cancer)
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L26 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:242436 HCAPLUS
DN 138:265693
ED Entered STN: 28 Mar 2003
TI **IGF-binding protein**-derived peptide or small molecule, and use thereof
IN Mascarenhas, Desmond
PA Bioexpertise, LLC, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 1-12 (**Pharmacology**)
Section cross-reference(s): 2
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003025121	A2	20030327	WO 2002-US25532	20020809 <--
	WO 2003025121	A3	20040122		
	W: AU, CA, JP				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
	EP 1435986	A2	20040714	EP 2002-759330	20020809 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
PRAI	US 2001-323267P	P	20010918 <--		
	WO 2002-US25532	W	20020809 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003025121	ICM	C12N

AB New compns. based on **IGF-binding protein** sequences are provided. New tools for high-throughput research are provided. New methods for the treatment of human disease are provided. **IGFBP-3**-derived peptide or small mol. is administered to subjects having disease, thereby alleviating the symptoms of the disease.

ST peptide **IGF binding protein** therapeutic
IT Allergy
Allergy inhibitors
Angiogenesis
Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antitumor agents
Apoptosis
Arthritis
Asthma
Autoimmune disease
Bone, disease
Cardiovascular agents
Cardiovascular system, disease
Fibrosis
Human
Inflammation
Lung, neoplasm
Mammary gland, neoplasm

Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Peptidomimetics
Prostate gland, neoplasm
Reproductive tract, disease
Stomach, neoplasm
(**IGF-binding protein**-derived peptide or small mol., and use)

IT Insulin-like growth factor-**binding proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF-binding protein**-derived peptide or small mol., and use)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF-binding protein**-derived peptide or small mol., and use)

IT Drug interactions
(**IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)

IT Fibrinogens
Fibronectins
Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)

IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(**IGFBP-3**; **IGF-binding protein**-derived peptide or small mol., and use)

IT Extracellular matrix
(binding; **IGF-binding protein**-derived peptide or small mol., and use)

IT Metals, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding; **IGF-binding protein**-derived peptide or small mol., and use)

IT Imaging
(cell; **IGF-binding protein**-derived peptide or small mol., and use)

IT Intestine, neoplasm
(colon; **IGF-binding protein**-derived peptide or small mol., and use)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression, expression tag properties; **IGF-binding protein**-derived peptide or small mol., and use)

IT Animal cell
(imaging; **IGF-binding protein**-derived peptide or small mol., and use)

IT Intestine, disease
(inflammatory; **IGF-binding protein** -derived peptide or small mol., and use)

IT Biological transport
(internalization; **IGF-binding protein** -derived peptide or small mol., and use)

IT Transcription, genetic
(modulation; **IGF-binding protein**-derived peptide or small mol., and use)

IT Eye, disease
(retinopathy, proliferative; **IGF-binding**

protein-derived peptide or small mol., and use)
IT Drug interactions
(synergistic; **IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)
IT 97162-88-4, 3C Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HRV; **IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)
IT 67763-96-6D, Insulin-like growth factor 1, complexes with **IGFBP3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF-binding protein**-derived peptide or small mol., and use)
IT 171022-91-6D, hexahistidine and green fluorescent protein conjugates
502845-66-1D, hexahistidine and green fluorescent protein conjugates
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(**IGF-binding protein**-derived peptide or small mol., and use)
IT 405276-09-7 405276-09-7D, peptidomimetic derivs. 405276-10-0
405276-10-0D, peptidomimetic derivs. 502845-62-7 502845-62-7D, peptidomimetic derivs. 502845-63-8 502845-63-8D, peptidomimetic derivs. 502845-64-9 502845-64-9D, peptidomimetic derivs. 502845-65-0
502845-65-0D, peptidomimetic derivs.
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF-binding protein**-derived peptide or small mol., and use)
IT 171022-91-6D, green fluorescent protein conjugates 502845-66-1
502845-66-1D, green fluorescent protein conjugates 502845-67-2D, green fluorescent protein conjugates 502845-68-3 502845-69-4 502845-70-7
502845-71-8 502845-72-9 502845-73-0 502845-74-1 502845-75-2
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(**IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)
IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 57-22-7, Vincristine
59-05-2, Methotrexate 10540-29-1, Tamoxifen 18883-66-4, Streptozotocin
23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)
IT 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies 7440-02-0, Nickel, biological studies 7440-48-4, Cobalt, biological studies 7440-66-6, Zinc, biological studies 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGFBP3** binding; **IGF-binding protein**-derived peptide or small mol., uses, and use with other agents)
IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition; **IGF-binding protein**-derived peptide or small mol., and use)
IT 503336-31-0 503336-32-1 503336-33-2 503336-34-3 503336-35-4
503336-36-5 503336-37-6 503336-38-7 503336-39-8 503336-40-1
RL: PRP (Properties)
(unclaimed sequence; **iGF-binding protein**-derived peptide or small mol., and use thereof)

L26 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:974059** HCAPLUS
DN **138:252574**

ED Entered STN: 26 Dec 2002
TI Clinical significance of **insulin-like growth factor-binding protein-3** expression in stage I non-small cell lung cancer
AU Chang, Yoon Soo; Gong, Koo; Sun, Shihua; Liu, Diane; El-Naggar, Adel K.; Khuri, Fadlo R.; Hong, Waun Ki; Lee, Ho-Young
CS Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Clinical Cancer Research (**2002**), 8(12), 3796-3802
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB The activities of insulin-like growth factors (**IGFs**), including mitogenic and antiapoptotic properties, are modulated by a family of high-affinity insulin-like growth factor-**binding proteins** (**IGFBPs**), of which **IGFBP-3** is the major serum carrier protein. Even though it is well known that **IGFBP-3** plays an important role in cell proliferation, the expression of **IGFBP-3** and its significance in primary nonsmall cell lung cancer (NSCLC) samples are unknown. This study explored **IGFBP-3** expression in tumor samples from 74 patients with a diagnosis of pathol. stage I NSCLC to determine if the expression status of IFGBP-3 influences the prognosis of patients with NSCLC. Two-sided statistical analyses were performed to correlate the clin. parameters and the prognostic effect with the **IGFBP-3** expression level in this cohort. Reduced **IGFBP-3** expression was found in 42 (56.8%) of 74 samples, and it was more frequent in large cell carcinoma than in squamous cell carcinoma and adenocarcinoma, although this difference was not statistically significant. This phenomenon was not associated with the other clinicopathol. parameters tested, such as age, sex, histol. grade, and smoking history. Significant statistical correlation between **IGFBP-3** expression and disease-specific survival was noted (P = 0.019 by log-rank test). Although statistically nonsignificant, patients with decreased **IGFBP-3** expression had shorter overall, disease-free, and event-free survival rates than did patients with normal **IGFBP-3** expression. In a multivariate anal. using **IGFBP-3** expression and other clinicopathol. parameters, the level of **IGFBP-3** expression remained as an independent factor for predicting a shorter disease-specific survival probability (P = 0.020). Our work demonstrates that down-regulation of **IGFBP-3** is a frequent event in stage I NSCLC and correlates with the disease-specific survival probability of patients with stage I NSCLC. These results suggest that **IGFBP-3** functions as a tumor suppressor and plays an important role in determining biol. aggressiveness in early NSCLC.
ST **IGFBP3** nonsmall cell lung cancer prognosis marker
IT Death
Human
Prognosis
Tumor markers
(**IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3**; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
IT **Lung, neoplasm**
(**adenocarcinoma**; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)

IT Bronchi
(epithelium; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
IT **Lung, neoplasm**
(**large-cell carcinoma**; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
IT **Lung, neoplasm**
(**non-small-cell carcinoma**; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
IT **Lung, neoplasm**
(**squamous cell carcinoma**; **IGFBP-3** expression as prognostic indicator in nonsmall cell lung cancer)
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L26 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:974042** HCAPLUS
DN **138:252564**

ED Entered STN: 26 Dec 2002
TI Correlation between **insulin-like growth factor-binding protein-3** promoter methylation and prognosis of patients with stage I non-small cell lung cancer
AU Chang, Yoon Soo; Wang, Luo; Liu, Diane; Mao, Li; Hong, Waun Ki; Khuri, Fadlo R.; Lee, Ho-Young
CS Departments of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Clinical Cancer Research (**2002**), 8(12), 3669-3675
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB Purpose: The activities of insulin-like growth factors (**IGFs**) in regulating cell proliferation, differentiation, and apoptosis are modulated by a family of high-affinity specific **IGF-binding proteins** (**IGFBPs**), especially **IGFBP-3**, the most abundant **IGFBP** in circulation. Hypermethylation of the promoter represses the expression of the **IGFBP-3** gene. The purpose of this study was to determine whether the methylation status of **IGFBP-3** promoter influences the prognosis of non-small cell lung cancer (NSCLC). Exptl. Design: Eighty-three patients with pathol. stage I NSCLC who had undergone curative surgery were investigated for promoter hypermethylation of **IGFBP-3** by methylation-specific PCR. Statistical analyses, all two-sided, were performed to determine the prognostic effect of methylation status of the **IGFBP-3** promoter on various clin. parameters. **IGFBP-3** was the only mol. parameter tested on these tissues in this study. Results: Hypermethylation of the **IGFBP-3** promoter was found in 51 (61.5%) of the 83 tumors. The clinicopathol. factors, such as age, histol. type, histol. grade, gender, and smoking status, of corresponding patients, did not exhibit statistically significant association with the methylation status of **IGFBP-3** promoter. However, patients with a hypermethylated **IGFBP-3** promoter had a significantly lower 5-yr disease-specific, disease-free, and overall survival rate than did those without a methylated **IGFBP-3** promoter (53.1% vs. 86.1%, P = 0.006; 36.5% vs. 76.2%, P = 0.007; and 38.9% vs. 64.0%, P = 0.022, resp.). Moreover, multivariate anal. indicated that hypermethylation of the **IGFBP-3** promoter was the only independent predictor for disease-free and disease-specific survival among the clin. and histol. parameters tested. Conclusions: Hypermethylation of the **IGFBP-3** promoter, as measured by methylation-specific PCR, is a frequent phenomenon and strongly associated with poor prognosis among patients with stage I NSCLC.
ST **IGFBP3** gene promoter methylation nonsmall cell lung cancer prognosis
IT Death
Human
Prognosis
Tumor markers
(**IGFBP-3** gene promoter methylation and prognosis of patients with stage I non-small cell lung cancer)
IT Promoter (genetic element)
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**IGFBP-3** gene promoter methylation and prognosis of patients with stage I non-small cell lung cancer)
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,

unclassified); PRP (Properties); BIOL (Biological study)
(**IGFBP-3**; **IGFBP-3** gene promoter
methylation and prognosis of patients with stage I non-small cell lung cancer)

IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGFBP-3**; **IGFBP-3** gene promoter
methylation and prognosis of patients with stage I non-small cell lung cancer)

IT **Lung, neoplasm**
(**adenocarcinoma**; **IGFBP-3** gene promoter
methylation and prognosis of patients with stage I non-small cell lung cancer)

IT DNA
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(hypermethylation; **IGFBP-3** gene promoter
methylation and prognosis of patients with stage I non-small cell lung cancer)

IT **Lung, neoplasm**
(**non-small-cell carcinoma**;
IGFBP-3 gene promoter methylation and prognosis of
patients with stage I non-small cell lung cancer)

IT **Lung, neoplasm**
(**squamous cell carcinoma**; **IGFBP**
-3 gene promoter methylation and prognosis of patients with
stage I non-small cell lung cancer)

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L26 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:716441 HCAPLUS
DN 137:242156
ED Entered STN: 20 Sep 2002
TI Peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof
IN Deshayes, Kurt; Lowman, Henry B.; Schaffer, Michelle L.; Sidhu, Sachdev S.
PA Genentech, Inc., USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 1-6 (**Pharmacology**)
Section cross-reference(s): 6

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002072780	A2	20020919	WO 2002-US7606	20020313 <--
	WO 2002072780	A3	20040108		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003092631	A1	20030515	US 2002-98093	20020313 <--
	EP 1401476	A2	20040331	EP 2002-717620	20020313 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-275904P	P	20010314 <--		
	WO 2002-US7606	W	20020313 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002072780	ICM	C12N

OS MARPAT 137:242156
AB Peptides are provided that antagonize the interaction of **IGF**-1 with its **binding proteins**, insulin receptor, and **IGF** receptor. These **IGF** antagonist peptides are useful in treating disorders involving **IGF**-1 as a causative agent, such as, for example, various cancers. The invention also provides conjugates comprising the peptide conjugated with a cytotoxic agent or polyethylene glycol. The cytotoxic agent here may be one that is active in killing

cells once internalized. Uses of these peptides include all uses that antagonize at least one biol. activity of exogenous or endogenous **IGFs.** They can be used in treating, inhibiting, or preventing conditions in which an **IGF** antagonist such as **IGFBP-3** or antibodies to **IGF**-1 is useful. The invention also provides a composition comprising one of the peptides described above in a carrier. Preferably, this composition is sterile and the carrier is a pharmaceutically acceptable carrier. Also preferred is the composition further comprising an angiogenic agent or chemotherapeutic agent, and also one that is suitable for injection or inhalation. A kit is also provided comprising a container containing the composition and instructions directing the

user to utilize the composition In a further preferred embodiment, before the administration step of the above method, the concentration of **IGF**-1 in a body sample from the mammal is measured, wherein an elevated concentration of **IGF**-1 above a reference range for **IGF**-1 indicates an increased risk for the disorder. The body sample is preferably selected from the group consisting of tumor tissue, blood, plasma, serum, mammary fluid, and seminal fluid. In another preferred embodiment, the **IGF**-1 is total **IGF**-1, free **IGF**-1 or complexed **IGF**-1, and the disorder is cancer, a diabetic complication exacerbated by **IGF**-1, preferably diabetic retinopathy or diabetic nephropathy, acromegaly, age-related macular degeneration, ischemic injury, or a trauma.

ST peptide antagonist insulin like growth factor **IGF** anticancer diagnosis

IT Disease, animal
(**IGF**-1 related, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT **Insulin-like growth factor-binding proteins**
RL: ARU (Analytical role, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**IGFBP-3**; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Blood
Blood plasma
Blood serum
Neoplasm
(body sample from; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Diagnosis
(cancer; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Drug delivery systems
(carriers; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Intestine, neoplasm
(colorectal, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Kidney, disease
(diabetic nephropathy, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Eye, disease
(diabetic retinopathy, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Mammary gland
Semen
(fluid, body sample from; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Drug delivery systems
(inhalants; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT Drug delivery systems
(injections; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Eye, disease
(macula, degeneration, age-related, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Diagnosis
(mol.; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Cytotoxic agents
(peptide antagonist conjugated with; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(peptide antagonist conjugated with; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Angiogenesis inhibitors
Antidiabetic agents
Antitumor agents
Chemotherapy
Human
Mammalia
Phage display library
Protein sequences
Test kits
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Amino acids, biological studies
Insulin-like growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Angiogenic factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Prostate-specific antigen
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Injury
(trauma, treatment of; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)
IT Acromegaly
Diabetes mellitus
Ischemia
Lung, neoplasm
Mammary gland, neoplasm
Prostate gland, neoplasm
(treatment of; peptide antagonist of insulin-like growth factor (

IGF) and therapeutic uses thereof)

IT 460323-60-8P 460323-61-9P 460323-62-0P 460323-63-1P 460323-64-2P
460396-78-5P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT 25322-68-3, Polyethylene glycol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(peptide antagonist conjugated with; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT 67763-96-6P, Insulin like growth factor 1
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT 460400-91-3 460400-92-4 460400-93-5 460400-94-6 460400-95-7
460400-96-8 460400-97-9 460400-98-0 460400-99-1 460401-00-7
460401-01-8 460401-02-9 460401-03-0 460401-04-1 460401-05-2
460401-06-3 460401-07-4 460401-08-5 460401-09-6 460401-10-9
460401-11-0 460401-12-1 460401-13-2 460401-14-3 460401-15-4
RL: PRP (Properties)
(unclaimed protein sequence; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

IT 121481-26-3 207220-79-9 460323-65-3 460323-66-4 460323-67-5
460323-68-6 460323-69-7 460323-70-0 460323-71-1 460323-72-2
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460323-83-5 460323-84-6 460323-85-7 460323-86-8 460323-87-9
460323-88-0 460323-89-1 460323-90-4 460323-91-5 460323-92-6
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460323-98-2 460323-99-3 460324-00-9 460324-01-0 460324-02-1
460324-03-2 460324-04-3 460324-05-4 460324-06-5 460324-07-6
460324-08-7 460324-09-8 460324-10-1 460324-11-2 460324-12-3
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460324-43-0 460324-44-1 460324-45-2 460324-46-3 460324-47-4
460324-48-5 460324-49-6 460324-50-9
RL: PRP (Properties)
(unclaimed sequence; peptide antagonist of insulin-like growth factor (**IGF**) and therapeutic uses thereof)

L26 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:625685** HCAPLUS
DN **137:333513**
ED Entered STN: 20 Aug 2002
TI **IGFBP-3** mediates p53-induced apoptosis during serum starvation
AU Grimberg, Adda; Liu, Bingrong; Bannerman, Peter; El-Deiry, Wafik S.; Cohen, Pinchas
CS Division of Pediatric Endocrinology, Abramson Research Center, The Children's Hospital of Philadelphia, Abramson Research Center, Philadelphia, PA, 19104, USA
SO International Journal of Oncology (**2002**), 21(2), 327-335
CODEN: IJONES; ISSN: 1019-6439
PB International Journal of Oncology

DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Insulin-like growth factor **binding protein** (**IGFBP**)-3, a p53-response gene, can induce apoptosis in an **IGF**-independent manner. Here we demonstrate that **IGFBP-3** mediates p53-induced apoptosis during serum starvation using two foil neoplastic cell models: one which introduces p53 activity and one which eliminates it. We created a doxycycline-inducible p53 model from the p53-neg. PC-3 prostate cancer cell line. Doxycycline treatment increased both p53 and **IGFBP-3** levels. It also augmented apoptosis, but not during insulin-like growth factor-I co-treatment. In a second model, lung carcinoma H460 cells expressing fully functional p53 were stably transfected with E6, which targets p53 for degradation H460-E6 cells contained less p53 and **IGFBP-3** than control neo-transfected cells, and proteasome blockade restored both. In serum deprivation, H460-E6 cells had enhanced growth and less apoptosis than did H460-neo cells. Redns. in H460-neo apoptosis, comparable in magnitude to H460-E6, were achieved by adding anti-**IGFBP-3**-antibody or **IGFBP-3** antisense oligomers, but not non-specific Ig or **IGFBP-3** sense oligomers. In summary, turning p53 'on' in two foil neoplastic cell models induced **IGFBP-3** expression and increased apoptosis during serum starvation, an effect inhibited by insulin-like growth factor-I treatment and specific **IGFBP-3** blockade. This is the first demonstration of inhibition of p53 action by antagonizing **IGFBP-3.**
ST **IGFBP3** p53 apoptosis blood starvation
IT Apoptosis
Blood serum
Human
Prostate gland, neoplasm
Signal transduction, biological
(**IGF**-BP-3 mediates p53-induced apoptosis during serum starvation)
IT p53 (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF**-BP-3 mediates p53-induced apoptosis during serum starvation)
IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGFBP-3**; **IGF-BP-3** mediates p53-induced apoptosis during serum starvation)
IT **Lung, neoplasm**
(**carcinoma**; **IGF**-BP-3 mediates p53-induced apoptosis during serum starvation)
IT 67763-96-6, **IGF**-I
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(doxycycline and **IGF**-I effect on **IGF**-BP-3 and p53 and apoptosis)
IT 564-25-0, Doxycycline
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(doxycycline elevation of **IGF**-BP-3 and p53 and apoptosis in prostate cancer cell line)
IT 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteasome regulation of **IGF**-BP-3 and p53 and apoptosis)
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L26 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:611558 HCAPLUS
DN 137:335861
ED Entered STN: 16 Aug 2002
TI What is the role of the insulin-like growth factor system in the pathophysiology of cancer cachexia, and how is it regulated?
AU Crown, A. L.; Cottle, K.; Lightman, S. L.; Falk, S.; Mohamed-Ali, V.; Armstrong, L.; Millar, A. B.; Holly, J. M. P.
CS Department of Medicine, University of Bristol, London, UK
SO Clinical Endocrinology (Oxford, United Kingdom) (**2002**), 56(6), 723-733
CODEN: CLECAP; ISSN: 0300-0664
PB Blackwell Science Ltd.
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2, **15**
AB OBJECTIVE AND BACKGROUND: The cancer cachexia syndrome is characterized by anorexia, weight loss with muscle wasting and increased energy expenditure. It is associated with increased morbidity and mortality, but its etiol. is poorly understood and no effective therapeutic intervention is available. It may result from an imbalance between the activity or effect of anabolic and catabolic hormones, mediated by the inflammatory cytokines. **IGF**-I is a potent anabolic agent, with therapeutic potential. Our objective was to investigate the role and regulation of the **IGF** system in cancer cachexia. DESIGN AND PATIENTS: We set up a prospective study of 30 patients with newly diagnosed unresectable non-small cell lung cancer, together with a cross-sectional comparison group of healthy

volunteers. MEASUREMENTS: We examined the relationship between aspects of the **IGF** system, including **IGFBP-3** proteolysis (using Western ligand and immunoblotting and an in vitro **IGFBP-3** protease assay); the inflammatory cytokines and their soluble receptors; and food intake and nutritional status (including biochem. and anthropometric assessments). RESULTS: Although we did not observe a marked reduction in food intake in the cancer patients, the majority lost weight and functionally important lean body mass. We observed GH resistance in the cancer patients, and intermittent proteolysis of **IGFBP-3**, which correlated with the circulating interleukin-6 (IL-6) concentration The pattern of **IGFBP-3** proteolysis was unusual, with a prominent 17-kDa fragment. Less **IGFBP-3** proteolysis was associated with more weight loss, suggesting that this could be a protective counter-regulatory mechanism, increasing **IGF**-I bioavailability to the tissues. CONCLUSIONS: Cancer cachexia in humans is a complex condition. Patients tend to be GH resistant. The significance of the intermittent increases in **IGFBP-3** proteolysis, which may be regulated by IL-6, remains uncertain. A better understanding of the pathophysiol. should enable the development of novel therapeutic approaches.

ST **IGF** IL6 TNFalpha GH resistance lung cancer cachexia

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C-reactive; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia in relation to)

IT **Insulin-like growth factor-binding proteins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**IGFBP-3**; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT Human
(altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT Interleukin 6
Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT Cachexia
(cancerous; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT **Lung, neoplasm**
(**non-small-cell carcinoma**; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT Protein degradation
(of **IGFBP-3**; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α via their receptors in human lung cancer cachexia)

IT Interleukin 6 receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(soluble; altered **IGF** system associated with GH resistance and

increased **IGFBP-3** proteolysis-induced by IL-6 and
TNF-α via their receptors in human lung cancer cachexia)
IT Tumor necrosis factor receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(type 1; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and
TNF-α via their receptors in human lung cancer cachexia)
IT Tumor necrosis factor receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(type 2; altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and
TNF-α via their receptors in human lung cancer cachexia)
IT 67763-96-6, **IGF**-I 67763-97-7, **IGF**-II 138069-94-0, **IGFBP-3** protease
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(altered **IGF** system associated with GH resistance and increased **IGFBP-3** proteolysis-induced by IL-6 and TNF-α
via their receptors in human lung cancer cachexia)
IT 9002-72-6, GH
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; altered **IGF** system associated with GH resistance
and increased **IGFBP-3** proteolysis-induced by IL-6
and TNF-α via their receptors in human lung cancer cachexia)
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L26 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:471949** HCAPLUS
DN **137:180178**
ED Entered STN: 24 Jun 2002
TI **Insulin-like growth factor binding protein**-3 inhibits the growth of non-small cell lung cancer
AU Lee, Ho-Young; Chun, Kyung-Hee; Liu, Bingrong; Wiehle, Sandra A.; Cristiano, Richard J.; Hong, Waun Ki; Cohen, Pinchas; Kurie, Jonathan M.
CS Departments of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Cancer Research (**2002**), 62(12), 3530-3537
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Insulin-like growth factors (**IGFs**) have mitogenic and antiapoptotic properties and have been implicated in the development of lung cancer. The effects of **IGFs** are modulated by **IGFBPs**. This study explored the effects of **IGFBP**-3 on non-small cell lung cancer (NSCLC) cells after infection with an adenovirus constitutively expressing **IGFBP-3** under the control of the cytomegalovirus promoter (Ad5CMV-BP3). The authors found that **IGFs**, especially **IGF**-I, stimulated the growth of NSCLC cells, and Ad5CMV-BP3 suppressed this **IGF**-I-induced NSCLC cell growth. They also found that the clonogenicity of H1299 cells in soft agar was markedly reduced by Ad5CMV-BP3. Furthermore, direct injection of Ad5CMV-BP3 into H1299 NSCLC xenografts s.c. established in athymic nude mice induced massive destruction of the tumors. Ad5CMV-BP3 did not induce detectable cytotoxicity on normal human bronchial epithelial cells, suggesting therapeutic efficacy of this virus. Ad5CMV-BP3 infection was accompanied by apoptotic cell death in vitro as detected by flow cytometry, DNA fragmentation anal., and Western blot anal. on the expression of Bcl-2 and on the cleavage of poly(ADP-ribose) polymerase, a substrate of caspase 3. Immunofluorescence confocal microscopy was also used to show the apoptotic effect of Ad5CMV-BP3 in H1299 tumors established in nude mice. These findings indicated that **IGFBP-3** was a potent inducer of apoptosis in NSCLC cells

in vitro and in vivo. To delineate the underlying mechanism, the authors examined the effect of **IGFBP-3** on Akt/protein kinase B and glycogen synthase kinase-3β, downstream mediators of the phosphatidylinositol 3-kinase pathway, and on mitogen-activated protein kinase (MAPK), all three of which are activated by **IGF**-mediated signaling pathways and have important roles in cell survival. **IGFBP-3** overexpression inhibited the phosphorylation of Akt and glycogen synthase kinase-3β and the activity of MAPK. Furthermore, **IGF**-I rescued the NSCLC cells from serum depletion-induced apoptosis, and this rescue was blocked in Ad5CMV-BP-3-infected H1299 NSCLC cells. Transient transfection with activated Akt or constitutively active MAPK kinase-1, an upstream activator of MAPK, partially blocked **IGFBP-3**-induced apoptosis of NSCLC cells. These findings suggested that the growth-regulatory effect of **IGFBP-3** on NSCLC cells was attributable in part to the inhibition of the **IGF**-induced survival pathway. These data demonstrate the importance of **IGFBP -3** in the regulation of NSCLC cell proliferation, clonogenicity, and tumor growth, suggesting that **IGFBP-3** is a target for the treatment of lung cancer and that Ad5CMV-BP3 is a potential therapeutic agent.

ST **IGFBP3** apoptosis nonsmall cell lung cancer; adenovirus vector **IGFBP3** therapy nonsmall cell lung cancer; phosphatidylinositol kinase MAPK lung cancer apoptosis **IGFBP3**

IT Animal cell line
(H1299; **IGF**-BP-3 inhibition of non-small cell lung cancer growth)

IT Antitumor agents
Apoptosis
Cell proliferation
Genetic vectors
Human
(**IGF**-BP-3 inhibition of non-small cell lung cancer growth)

IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3**; **IGF-BP-3**
inhibition of non-small cell lung cancer growth)

IT **Lung, neoplasm**
(**non-small-cell carcinoma**;
IGF-BP-3 inhibition of non-small cell lung cancer growth)

IT 9059-09-0, Glycogen synthase kinase 67763-96-6, **IGF**-1
115926-52-8, Phosphatidylinositol 3-kinase 142243-02-5, MAP kinase
142805-58-1, MEK-1 kinase 148640-14-6, Akt kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF**-BP-3 inhibition of non-small cell lung cancer growth)

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L26 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:240579 HCAPLUS
DN 136:273173
ED Entered STN: 28 Mar 2002
TI Method for use of **IGF-binding protein** for selective sensitization of target cells in vivo
IN Mascarenhas, Desmond
PA Bioexpertise, LLC, USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC 1-6 (**Pharmacology**)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002024216	A2	20020328	WO 2001-US29188	20010918 <--
	WO 2002024216	A3	20040715		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001091090	A5	20020402	AU 2001-91090	20010918 <--
	US 2003035788	A1	20030220	US 2001-956508	20010918 <--
PRAI	US 2000-233840P	P	20000919	<--	
	WO 2001-US29188	W	20010918	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002024216	ICM	A61K038-00

AB Methods for the treatment of human disease are provided. **IGFBP-3** is administered together with a co-administered agent to

subjects having disease, thereby alleviating the symptoms of the disease, under conditions where administration of **IGFBP-3** alone at the maximum practicable dose has no measurable beneficial effect on the disease condition.

ST **IGFBP3** insulin **binding protein** sequence
antitumor

IT **Insulin-like growth factor-binding proteins**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGFBP-3**; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Mammary gland
(adenocarcinoma, inhibitors; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antitumor agents
(antibiotic; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Nutrients
(antinutrients; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antibiotics
(antitumor; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Intestine, neoplasm
(colon, inhibitors; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antitumor agents
(colon; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT **Lung, neoplasm**
Pancreas, neoplasm
Stomach, neoplasm
(inhibitors; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligands; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antitumor agents
(lung; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antitumor agents
(mammary gland adenocarcinoma; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Acidity
Alkylating agents, biological
Antitumor agents
Apoptosis
Heat
Human
Osmolarity
Pressure
Protein sequences
Radiation
Test kits
Vaccines
(method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

IT Antibodies and Immunoglobulins

DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for use of **IGF-binding protein**
for selective sensitization of target cells in vivo)
IT Cytokines
Nucleic acids
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for use of **IGF-binding protein**
for selective sensitization of target cells in vivo)
IT Prostate gland
(neoplasm, inhibitors; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT Antitumor agents
(pancreas; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT Antitumor agents
(prostate gland; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT Microtubule
(stabilizer; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT Antitumor agents
(stomach; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT 405341-12-0 405341-13-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)
IT 169592-56-7, Caspase-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for use of **IGF-binding protein**
for selective sensitization of target cells in vivo)
IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 59-05-2, Methotrexate 518-28-5D, Podophyllotoxin, analogs 10540-29-1, Tamoxifen 13010-20-3, Nitrosourea 15663-27-1, Cisplatin 18883-66-4, Streptozotocin 25316-40-9, Adriamycin 33069-62-4, Taxol 33419-42-0, Etoposide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for use of **IGF-binding protein**
for selective sensitization of target cells in vivo)
IT 405276-09-7 405276-10-0
RL: PRP (Properties)
(unclaimed sequence; method for use of **IGF-binding protein** for selective sensitization of target cells in vivo)

L26 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:850890 HCAPLUS
DN 136:1666
ED Entered STN: 23 Nov 2001
TI cDNA and polypeptide sequences for human **insulin-like growth factor binding protein**
3 receptor (**IGF**-BP-3R), an **IGF**-independent
IGFBP-3 interacting protein, and their diagnostic and

therapeutic uses
IN Oh, Youngman; Rosenfeld, Ron; Ingermann, Angela Ranae
PA Oregon Health & Sciences University, USA
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): **1**, 2, 9, 13, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087238	A2	20011122	WO 2001-US16437	20010517 <--
	WO 2001087238	A3	20020606		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001064769	A5	20011126	AU 2001-64769	20010517 <--
	EP 1290162	A2	20030312	EP 2001-939229	20010517 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004072285	A1	20040415	US 2003-276491	20030220 <--
PRAI	US 2000-204949P	P	20000517 <--		
	WO 2001-US16437	W	20010517 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001087238	ICM	A61K

AB There is disclosed an isolated cDNA sequence (SEQ ID NO:1), clone 4.33, encoding a polypeptide and comprising a coding region (SEQ ID NO:2) of the sequence described in SEQ ID NO:1, or a sequence having at least 90% homol. with the coding region of SEQ ID NO:1. The clone 4.33 polypeptide functions as a specific cell-surface receptor for **IGF**-BP-3 (**insulin-like growth factor binding protein 3**), and undergoes nuclear translocation in combination with **IGF**-BP-3. **IGF**-BP-3 and **IGF**-BP-3R (**insulin-like growth factor binding protein 3** receptor P4.33) cooperatively suppress DNA synthesis and cell growth, and induce caspase activation and apoptosis in cancer cells, indicating that clone 4.33 is an important mediator of **IGF**-independent growth inhibitory actions of **IGF**-BP-3. The P4.33:**IGFBP-3** system of the present invention can be used, inter alia, in screening and diagnostic assays, and for therapeutic methods for cancer treatment and tumor suppression. CDNA clone 4.33 is expressed in multiple human tissues and is differentially expressed in normal vs. cancerous human cell lines. There is a significant decrease in endogenous expression of clone 4.33 in PC-3 prostate cancer cells. Exptl. results from overexpression of **IGF**-BP-3R in cancer cell lines suggest that it represents a novel mammalian cell death receptor.
ST cDNA sequence human **IGFBP 3** receptor; insulin like growth factor **binding protein** receptor drug screening; **IGFBP3R** binding **IGFBP** inhibition DNA replication cell proliferation; apoptosis cancer cell growth inhibition **IGFBP3** receptor diagnosis therapy
IT Cyclins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D1, cell differentiation marker; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Cyclins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, cell differentiation marker; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Animal cell line
(Hs578T (breast cancer), transfected; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Antisense oligonucleotides
Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF**-BP-3R-specific; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Receptors
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**IGF**-BP-3R; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT **Insulin-like growth factor-binding proteins**
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**IGFBP-3**; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Animal cell line
(MCF-7, transfected; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Animal cell line
(PC-3; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(RAP1, phosphorylation of, assays; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rb, cell differentiation marker; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Diagnosis
(agents; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Amniotic fluid
Lymph
Saliva
(anal.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(anti-**IGF**-BP-3R; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Apoptosis
Cell proliferation
Signal transduction, biological
Transcriptional regulation
Translation, genetic
(assays; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Antitumor agents
Blood analysis
Cell membrane
Diagnosis
Drug screening
Fluorescent indicators
Gene therapy
Immobilization, molecular or cellular
Immunotherapy
Lung, neoplasm
Mammary gland, neoplasm
Molecular association
Molecular cloning
Nucleic acid hybridization
PCR (polymerase chain reaction)
Prognosis
Protein sequences

Urine analysis
cDNA sequences
(cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT mRNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Diagnosis
Diagnosis
(cancer; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Prostate gland, neoplasm
(carcinoma; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Uterus, neoplasm
(cervix; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Intestine, neoplasm
(colon; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Immunoassay
(enzyme-linked immunosorbent assay; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized, monoclonal; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Enzymes, biological studies

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immobilized, label; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Immunoassay
(immunoblotting; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Drug delivery systems
(immunoconjugates; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Diagnosis
(immunodiagnosis; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Immunoassay
(immunohistochem.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Immunoassay
(immunopptn.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Biological transport
(intracellular, nuclear translocation assay; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Peptides, biological studies
Proteins
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(labeled; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Cell differentiation
(marker assay; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Diagnosis
(mol.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an

IGF-independent **IGFBP-3** interacting
protein, and their diagnostic and therapeutic uses)

IT Antibodies and Immunoglobulins
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; cDNA and polypeptide sequences for human **insulin -like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p21CIP1, cell differentiation marker; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Ras proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphorylation of, assays; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Phosphorylation, biological
(protein, receptor-mediated; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT DNA formation
(replication, inhibition of; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Placenta
Umbilical cord
(tissue, anal.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Cell nucleus
(translocation assay; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT Placenta
(villus, tissue, anal.; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF -BP-3R**), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT 251929-01-8P
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; cDNA and polypeptide sequences for human

insulin-like growth factor
binding protein 3 receptor (**IGF**
-BP-3R), an **IGF**-independent **IGFBP-3**
interacting protein, and their diagnostic and therapeutic uses)

IT 67763-96-6, **IGF**-I 67763-97-7, **IGF**-II
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT 186322-81-6, Caspase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell differentiation marker; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT 375927-99-4, 3: PN: WO0187238 SEQID: 3 claimed DNA 375928-00-0, 4: PN: WO0187238 SEQID: 4 claimed DNA 375928-01-1, 5: PN: WO0187238 SEQID: 5 claimed DNA 375928-02-2, 6: PN: WO0187238 SEQID: 6 claimed DNA 375928-03-3, 7: PN: WO0187238 SEQID: 7 claimed DNA 375928-04-4, 8: PN: WO0187238 SEQID: 8 claimed DNA 375928-05-5, 9: PN: WO0187238 SEQID: 9 claimed DNA 375928-06-6, 10: PN: WO0187238 SEQID: 10 claimed DNA 375928-07-7, 11: PN: WO0187238 SEQID: 11 claimed DNA 375928-08-8, 12: PN: WO0187238 SEQID: 12 claimed DNA 375928-09-9, 13: PN: WO0187238 SEQID: 13 claimed DNA 375928-10-2, 14: PN: WO0187238 SEQID: 14 claimed DNA 375928-11-3, 15: PN: WO0187238 SEQID: 15 claimed DNA 375928-12-4, 16: PN: WO0187238 SEQID: 16 claimed DNA 375928-13-5, 17: PN: WO0187238 SEQID: 17 claimed DNA
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **IGF**-BP-3 receptor specific antisense oligonucleotide; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R) and their diagnostic and therapeutic uses)

IT 375927-98-3
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

IT 142008-29-5, Protein kinase A 142243-02-5, MAP kinase 142805-58-1, Mek kinase 144697-16-5, B-Raf kinase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphorylation of, assays; cDNA and polypeptide sequences for human **insulin-like growth factor binding protein 3** receptor (**IGF**-BP-3R), an **IGF**-independent **IGFBP-3** interacting protein, and their diagnostic and therapeutic uses)

L26 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:213653** HCAPLUS
DN **135:178662**
ED Entered STN: 26 Mar 2001
TI Molecular pathology of lung cancer and the system of insulin-like growth factors

AU Kogan, E. A.; Jaques, G.
CS I. M. Sechenov Moscow Med. Academy, Moscow, 119881, Russia
SO Arkhiv Patologii (**1999**), 61(5), 55-61
CODEN: ARPTAF; ISSN: 0004-1955
PB Meditsina
DT Journal
LA Russian
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Mol. pathol. of lung cancer (LC) investigates mol.-genetic rearrangements initiating development and growth of the tumor. The system of insulin-like growth factors (**IGF**) and **binding proteins** (**IGFBP**) regulates cell proliferation in the majority of embryonal and tumor tissues of man and animals in the course of reparation processes and productive inflammatory reaction. A general property of all LC histol. types is the presence in their cells of various members of **IGF**-system. Content of IGFII in tumor cells correlated with **IGFBP**-1, **IGFBP**-2, **IGFBP**-5. Localization of IGFII and **IGFBP** in LC was different. **IGFBP**-1, -2, and -5, blocking IGFII, are detected in large amts. in areas of cell death inducing apoptosis while IGFII accumulates in dividing cells and foci of keratinization. Nuclear deposits of **IGFBP-3** in bronchioloalveolar LC create phenomenon of intranuclear inclusion of "owl's eye" type. Synthesis of the majority of **IGF** occurs in tumor cells. Stromal cells also produce and transport of IGFII and **IGFBP** into the tumor.
ST insulin like growth factor IGFII lung cancer; **IGFBP** lung cancer cell proliferation apoptosis
IT Insulin-like growth factor-**binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF**-BP-1; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Insulin-like growth factor-**binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF**-BP-2; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Insulin-like growth factor-binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF-BP-3**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Insulin-like growth factor-**binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF**-BP-4; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Insulin-like growth factor-**binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF**-BP-5; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)

IT Insulin-like growth factor-**binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF**-BP-6; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Cell nucleus
Cytoplasm
Extracellular matrix
Fibroblast
Histiocyte
Lymphocyte
(IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Apoptosis
Cell proliferation
(IGFII and **IGF-binding protein** localization in in different types of human lung cancer in relation to)
IT **Lung, neoplasm**
(**adenocarcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Lung, neoplasm**
(**carcinoid**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Bronchi**
(**carcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Blood vessel
(endothelium; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Lung, neoplasm**
(**large-cell carcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Lung, neoplasm**
(**non-small-cell carcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT Lymphocyte
(plasma cell; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Lung, neoplasm**
(**small-cell carcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT **Lung, neoplasm**
(**squamous cell carcinoma**; IGFII and **IGF-binding protein** localization in in different types of human lung cancer)
IT 67763-97-7, IGFII
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(IGFII and **IGF-binding protein** localization in in different types of human lung cancer)

L26 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:716902** HCAPLUS
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ED Entered STN: 11 Oct 2000
TI Role of the insulin-like growth factor family in cancer development and progression
AU Yu, Herbert; Rohan, Thomas
CS Feist-Weiller Cancer Center, Louisiana State University Health Sciences Center, Shreveport, LA, 71130-3932, USA
SO Journal of the National Cancer Institute (**2000**), 92(18), 1472-1489
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB A review with ~ 316 refs. The insulin-like growth factors (**IGFs**) are mitogens that play a pivotal role in regulating cell proliferation, differentiation, and apoptosis. The effects of **IGFs** are mediated through the **IGF**-I receptor, which is also involved in cell transformation induced by tumor virus proteins and oncogene products. Six **IGF-binding proteins** (**IGFBPs**) can inhibit or enhance the actions of **IGFs**. These opposing effects are determined by the structures of the **binding proteins**. The effects of **IGFBPs** on **IGFs** are regulated in part by **IGFBP** proteases. Laboratory studies have shown that **IGFs** exert strong mitogenic and antiapoptotic actions on various cancer cells. **IGFs** also act synergistically with other mitogenic growth factors and steroids and antagonize the effect of antiproliferative mols. on cancer growth. The role of **IGFs** in cancer is supported by epidemiol. studies, which have found that high levels of circulating **IGF**-I and low levels of **IGFBP-3** are associated with increased risk of several common cancers, including those of the prostate, breast, colorectum, and lung. Evidence further suggests that certain lifestyles, such as one involving a high-energy diet, may increase **IGF**-I levels, a finding that is supported by animal expts. indicating that **IGFs** may abolish the inhibitory effect of energy restriction on cancer growth. Further investigation of the role of **IGFs** in linking high energy intake, increased cell proliferation, suppression of apoptosis, and increased cancer risk may provide new insights into the etiol. of cancer and lead to new strategies for cancer prevention.
ST review **IGF IGFBP3** cancer
IT **Insulin-like growth factor-binding proteins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF-BP-3**; role of insulin-like growth factor family in cancer development and progression)
IT Prostate gland
(carcinoma; role of insulin-like growth factor family in cancer development and progression)
IT Mammary gland
(neoplasm; role of insulin-like growth factor family in cancer development and progression)
IT **Lung, neoplasm**
Neoplasm
Risk assessment
(role of insulin-like growth factor family in cancer development and progression)
IT 61912-98-9, Insulin like growth factor
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(role of insulin-like growth factor family in cancer development and progression)

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L26 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:678596** HCAPLUS
DN **133:294469**
ED Entered STN: 27 Sep 2000
TI Transfection of human **insulin-like growth factor-binding protein 3** gene inhibits cell growth and tumorigenicity: a cell culture model for lung cancer
AU Hochscheid, R.; Jaques, G.; Wegmann, B.
CS Department of Internal Medicine, Division of Hematology/Oncology, Philipps-University, Marburg, D-35033, Germany
SO Journal of Endocrinology (**2000**), 166(3), 553-563
CODEN: JOENAK; ISSN: 0022-0795
PB Society for Endocrinology
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB **IGF**-I and **IGF**-II are potent mitogens, postulated to exert autocrine/paracrine effects on growth regulation in human lung cancer. Their proliferative effects are modulated by **IGF-binding proteins** (**IGFBPs**), which are found in conditioned medium (CM) of lung cancer cell lines. The biol. role of the **IGFBPs**, which are ontogenetically and hormonally regulated, is not fully understood. Both inhibitory and stimulatory effects on cell growth have been demonstrated. Exogenous **IGFBP-3** has been consistently shown to block **IGF** action, inhibiting cell growth in vitro. In order to evaluate the action of endogenously produced **IGFBP-3** on cell growth in lung cancer, we stably transfected the non-small cell lung cancer cell line NCI-H23 with human **IGFBP-3** cDNA (resulting in NCI-H23 pOPI3/BP-3) or with the vector pOPI3CAT as control (resulting in NCI-H23 pOPI3CAT). RT-PCR confirmed expression of **IGFBP-3**-specific mRNA in NCI-H23 pOPI3/BP-3, but not in NCI-H23 or NCI-H23 pOPI3CAT. Western ligand blot and Western immunoblot anal. of CMs yielded strong signals of the characteristic 40-44 kDa human **IGFBP-3** protein in NCI-H23 pOPI3/BP-3. An **IGFBP-3** ELISA demonstrated a 20-fold increase in **IGFBP-3** protein expression in NCI-H23 pOPI3/BP-3 as compared with NCI-H23. The growth of NCI-H23 pOPI3/BP-3 in serum-containing medium was significantly slower (1.7-fold) than that of NCI-H23 or the vector-transfected control NCI-H23 pOPI3CAT. While the proliferation rate of parental and vector-transfected cells could be stimulated by **IGF**-I, **IGF**-II, **IGF**-I analog Long R3 **IGF**-I or insulin, that of NCI-H23 pOPI3/BP-3 could not. Xenotransplantation in nude mice resulted in a marked tumor growth after the injection of NCI-H23 or NCI-H23 pOPI3CAT, but absent or minimal growth for the **IGFBP-3**-transfected cell line. These data suggest that **IGFBP-3** is a potent inhibitor of cell growth in human lung cancer cell lines and may impair tumorigenicity in vivo.
ST **IGFBP3** lung cancer cell growth tumorigenicity
IT **Insulin-like growth factor-binding proteins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF-BP-3**; transfection of human **insulin-like growth factor-binding protein 3** gene inhibits cell growth and tumorigenicity: a cell culture model for lung cancer)

IT **Lung, neoplasm**
(**non-small-cell carcinoma**;
transfection of human **insulin-like growth**
factor-binding protein 3 gene
inhibits cell growth and tumorigenicity: a cell culture model for lung
cancer)
IT Proliferation inhibition
(transfection of human **insulin-like growth**
factor-binding protein 3 gene
inhibits cell growth and tumorigenicity: a cell culture model for lung
cancer)
IT 9004-10-8, Insulin, biological studies 67763-96-6, **IGF**-I
67763-97-7, **IGF**-II 143045-27-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(transfection of human **insulin-like growth**
factor-binding protein 3 gene
inhibits cell growth and tumorigenicity: a cell culture model for lung
cancer)
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AN **2000:370424** HCAPLUS
DN **133:264860**

ED Entered STN: 05 Jun 2000
TI Joint effect of insulin-like growth factors and mutagen sensitivity in lung cancer risk
AU Wu, Xifeng; Yu, He; Amos, Christopher I.; Hong, Waun K.; Spitz, Margaret R.
CS Department of Epidemiology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Journal of the National Cancer Institute (**2000**), 92(9), 737-743
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Background: We hypothesize that accumulation of genetic damage is dependent on an individual's intrinsic carcinogen sensitivity and on various humoral factors (e.g., insulin-like growth factors [**IGFs**]) that enhance proliferation, resistance to apoptotic cell death, and clonal outgrowth of genetically damaged cells. We tested this hypothesis by determining whether proliferation potential and genetic instability are associated with the risk of lung cancer. Methods: In a study of 183 lung cancer patients and 227 matched control subjects, we examined the joint effects of latent genetic instability (measured as mutagen sensitivity) and elevated proliferation potential (assessed by measuring **IGFs**) in lung cancer risk. Levels of **IGF**-I, **IGF**-II, and **IGF-binding protein**-3 (**IGFBP-3**) in plasma were measured by use of immunoassay kits. Mutagen sensitivity was assessed by quantitating bleomycin- and benzo[a]pyrene diol epoxide (BPDE)-induced chromatid breaks in peripheral blood lymphocyte cultures. Results: Although not statistically significant, the mean levels of **IGF**-I and the molar ratio of **IGF**-I/**IGFBP-3** were higher in patients with advanced or poorly differentiated disease than in patients with early or well-differentiated disease. Variation in **IGFs** was not associated with any specific histol. type or tumor stage. High levels of **IGF**-I and enhanced mutagen sensitivity were individually associated with increased risk of lung cancer: odds ratio (OR) of 2.13 (95% confidence interval [CI] = 1.20-3.78) for **IGF**-I, 2.50 (95% CI = 1.49-4.20) for bleomycin sensitivity, and 2.95 (95% CI = 1.72-5.06) for BPDE sensitivity. The OR was statistically significantly elevated to 8.88 for both higher **IGF**-I and bleomycin sensitivity (95% CI = 3.67-21.50) and to 13.53 for higher **IGF**-I and BPDE sensitivity combined (95% CI = 4.48-40.89). With all three risk factors considered together, the OR was 17.09 (95% CI = 4.16-70.27). High levels of **IGFBP-3** alone were associated with reduced lung cancer risk: OR = 0.59 (95% CI = 0.33-1.05). Conclusions: Our data suggest that individuals with genetic instability and higher proliferation potential are at enhanced risk for lung cancer.
ST **IGF IGFBP** mutagen sensitivity lung cancer risk
IT **Insulin-like growth factor-binding proteins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**IGF-BP-3**; insulin-like growth factors and mutagen sensitivity in human lung cancer risk)
IT **Lung, neoplasm**
(**adenocarcinoma**; insulin-like growth factors and mutagen sensitivity in human lung cancer risk)
IT Biomarkers (biological responses)
Blood plasma
Cell proliferation
Lung, neoplasm
Risk assessment
(insulin-like growth factors and mutagen sensitivity in human lung cancer risk)

IT **Lung, neoplasm**
(**large-cell carcinoma**; insulin-like
growth factors and mutagen sensitivity in human lung cancer risk)
IT **Lung, neoplasm**
(**small-cell carcinoma**; insulin-like
growth factors and mutagen sensitivity in human lung cancer risk)
IT **Lung, neoplasm**
(**squamous cell carcinoma**; insulin-like
growth factors and mutagen sensitivity in human lung cancer risk)
IT 11056-06-7, Bleomycin 58917-67-2
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(insulin-like growth factors and mutagen sensitivity in human lung
cancer risk)
IT 67763-96-6, **IGF**-I 67763-97-7, **IGF**-II
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU
(Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(insulin-like growth factors and mutagen sensitivity in human lung
cancer risk)
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AN **1999:788286** HCAPLUS
DN **132:18926**
ED Entered STN: 14 Dec 1999
TI **IGFs** and human cancer. Implications regarding the risk of growth hormone therapy
AU Shim, Melanie; Cohen, Pinchas
CS Division Pediatric Endocrinology, UCLA, Los Angeles, CA, 90095, USA
SO Hormone Research (**1999**), 51(Suppl. 3), 42-51
CODEN: HRMRA3; ISSN: 0301-0163
PB S. Karger AG
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 14
AB A review with 91 refs. is given. Perturbations of the insulin-like growth factor (**IGF**) axis, including the autocrine production of **IGFs**, **IGF binding proteins** (**IGFBPs**) and **IGFBP** proteases such as prostate specific antigen (PSA), and cathepsin D were identified in prostate, lung, and breast cancer cells and tissues. Blood serum **IGFBP-3** levels were found to be neg. correlated to the risk of cancer. Interestingly, **IGFBP-3** is a potent inhibitor of **IGF** action and also mediates apoptosis via an **IGF** -independent mechanism. Recent case-control studies have found an approx. 10% increase in the serum levels of **IGF**-I in patients with prostate, breast, and lung cancers, which are among the most frequently diagnosed cancers. While the studies indicate an association between serum **IGF**-I levels and cancer risk, causality was not established. Thus, serum **IGF**-I level may actually be a confounding variable, serving as a marker for autocrine tissue **IGF**-I production Growth hormone (GH) therapy raises both **IGF**-1 and **IGFBP**-3 levels in serum. However, the role of GH in controlling prostate, breast, and lung growth and carcinogenesis remains unclear from animal studies. Increased GH levels as seen in acromegaly were associated with benign prostatic hyperplasia but not with prostate, breast, or lung cancers, although colon cancer mortality may be increased. Should serum **IGF**-I levels be proven to play a causal role in the pathogenesis of cancer, interpreting the risk associated with therapies such as GH replacement must take into account both the duration of exposure and the risk magnitude associated with the degree of serum **IGF**-I elevation. Since GH-deficient patients often have a subnormal **IGF**-I serum level, which normalizes on therapy, their cancer risk on GH therapy probably does not increase substantially above that of the normal population. Until further research in the area dictates otherwise, ongoing surveillance and routine monitoring of **IGF**-I levels in GH recipients should become standard of care.
ST review **IGF IGFBP** growth hormone cancer
IT **Insulin-like growth factor-binding proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF-BP-3**; **IGFs** and cancer, risk of growth hormone therapy)
IT **Lung, neoplasm**
(**IGFs** and cancer, risk of growth hormone therapy)
IT Mammary gland
Prostate gland
(neoplasm; **IGFs** and cancer, risk of growth hormone therapy)
IT 67763-96-6, **IGF**-I

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGFs** and cancer, risk of growth hormone therapy)
IT 9002-72-6, Somatotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(replacement therapy; **IGFs** and cancer, risk of growth hormone therapy)
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L26 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1997:206468** HCAPLUS
DN **126:291716**
ED Entered STN: 29 Mar 1997
TI Nuclear localization of **insulin-like growth factor binding protein 3** in a lung cancer cell line
AU Jaques, Gabriele; Noll, Katja; Wegmann, Barbara; Witten, Sonja; Kogan, Eugenija; Radulescu, Razvan T.; Havemann, Klaus
CS Dep. Internal Med., Philipps-Univ., Marburg, D-35033, Germany
SO Endocrinology (**1997**), 138(4), 1767-1770
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Considerable evidence exists that lung cancer cell lines produce large amts. of insulin-like growth factor-**binding proteins** (**IGFBPs**). In addition, these cells are subject to an autocrine or

paracrine growth control by insulin-like growth factors (**IGFs**). The authors now demonstrate by immunocytochem. with **IGFBP-3** antibodies that nuclei of a lung cancer cell line (A549) distinctly immunostain for **IGFBP-3**. This finding led the authors to investigate in more detail the localization of this protein that, to date, had only been known to occur extracellularly. Ligand blotting revealed that purified nuclear exts. contain a 43,000-Da **IGFBP** which can bind [I125]**IGF**-I. By Western blot this protein was identified as **IGFBP-3**. Thus, the authors' data are consistent with the results of a previous structural study predicting a nuclear localization for **IGFBP-3**. Moreover, the authors' findings raise the possibility that nuclear **IGFBP-3** is functional and involved in the pathogenesis of lung cancer.

ST nucleus **IGFBP3** lung cancer

IT Animal cell line
(A549; nuclear localization of **insulin-like growth factor binding protein 3** in a lung cancer cell line)

IT **Insulin-like growth factor-binding proteins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**IGF-BP-3**; nuclear localization of **insulin-like growth factor binding protein 3** in a lung cancer cell line)

IT Cell nucleus
Lung, neoplasm
(nuclear localization of **insulin-like growth factor binding protein 3** in a lung cancer cell line)

IT 67763-96-6, **IGF**-I
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nuclear localization of **insulin-like growth factor binding protein 3** in a lung cancer cell line)

L26 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1996:412788** HCAPLUS
DN **125:77381**
ED Entered STN: 16 Jul 1996
TI Insulin-like growth factors stimulate the release of **insulin-like growth factor-binding protein-3** (**IGFBP-3**) and degradation of **IGFBP-4** in nonsmall cell lung cancer cell lines
AU Noll, Katja; Wegmann, Barbara R.; Havemann, Klaus; Jaques, Gabriele
CS Department of Internal Medicine, Philipps University Marburg, Marburg, 35043, Germany
SO Journal of Clinical Endocrinology and Metabolism (**1996**), 81(7), 2653-2662
CODEN: JCEMAZ; ISSN: 0021-972X
PB Endocrine Society
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 14
AB Insulin-like growth factors (**IGFs**) are potent mitogens for lung cancer cells. This proliferative activity is influenced by their **binding proteins** (**IGFBPs**). We report here on the regulatory effects of **IGF**-I and **IGF**-II on the production and release of **IGFBPs** by nonsmall cell lung cancer cell lines (NSCLC). The nine NSCLC cell lines used in this study showed mRNA

expression of all six **IGFBPs** known, as determined by PCR, and protein secretion of **IGFBP**-1, -2, -3, -4, and -6, as analyzed by Western immunoblots. The addition of **IGFs** to a serum-free medium showed divergence effects on **IGFBP**-3 and **IGFBP**-4 levels in a conditioned medium (GM). **IGF**-I and **IGF** -II, but not insulin, led to a much higher concentration of **IGFBP**-3 in the CM of all tested NSCLC cell lines, whereas the level of immunol. detected membrane-associated **IGFBP**-3 was decreased. Furthermore, Northern anal. of mRNA isolated from A549 revealed that **IGFBP**-3 specific mRNA was not changed by **IGF**-I or **IGF**-II, suggesting that the **IGF** -induced effects on **IGFBP**-3 depend on the release of cell-associated **IGFBP**-3. In contrast, **IGFBP**-4 levels were diminished by increasing concns. of **IGFs** in the CM of the NSCLCs A549, NCI-H157, and U1752, with no response to insulin or the **IGF**-I analog, whereas **IGFBP**-4-specific mRNA was not changed by **IGF**-I or **IGF**-II, as determined by Northern anal. The same effects were seen in a cell-free system after incubation of the CM with **IGFs**. The decrease in **IGFBP**-4 concns. was prevented by coincubation of the CM with the **IGFs** and either ethylenediamine tetraacetate or 1,10-phenanthrolene, but not with other protease inhibitors. We suggest that **IGFs** may either activate an **IGFBP**-4-specific metalloprotease present in NSCLC CM or that the binding of **IGFs** to **IGFBP**-4 may enhance the susceptibility of **IGFBP**-4 to proteolytic degradation Based on these data, we present evidence that **IGFs** may regulate their own availability both by releasing **IGFBP**-3 from cell membranes and through proteolytic degradation of **IGFBP**-4.

ST **IGF IGFBP3** IGFBP4 lung cancer

IT Transcription, genetic
(**IGF** stimulation of **IGF**-BP-3 release and **IGF**-BP-4 degradation in nonsmall cell lung cancer cell lines)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**IGF**-BP-1 (insulin-like growth factor-**binding protein** 1), **IGF** effect on **IGF**-BP-3 expression and metabolism in nonsmall cell lung cancer cell lines)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**IGF**-BP-2 (insulin-like growth factor-**binding protein** 2), **IGF** effect on **IGF**-BP-3 expression and metabolism in nonsmall cell lung cancer cell lines)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**IGF**-BP-3 (**insulin-like growth factor-binding protein** 3), **IGF** stimulation of **IGF**-BP-3 release and **IGF** -BP-4 degradation in nonsmall cell lung cancer cell lines)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**IGF**-BP-4 (insulin-like growth factor-**binding protein** 4), **IGF** stimulation of **IGF**-BP-3 release and **IGF**-BP-4 degradation in nonsmall cell lung cancer cell lines)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); PROC (Process)
IGF-BP-5 (insulin-like growth factor-**binding protein** 5), **IGF** effect on **IGF**-BP-3 expression and metabolism in nonsmall cell lung cancer cell lines)
IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
IGF-BP-6 (insulin-like growth factor-**binding protein** 6), **IGF** effect on **IGF**-BP-3 expression and metabolism in nonsmall cell lung cancer cell lines)
IT **Lung, neoplasm**
(non-small-cell carcinoma, **IGF** stimulation of **IGF**-BP-3 release and **IGF**-BP-4 degradation in nonsmall cell lung cancer cell lines)
IT 67763-96-6, **IGF**-I 67763-97-7, **IGF**-II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**IGF** stimulation of **IGF**-BP-3 release and **IGF**-BP-4 degradation in nonsmall cell lung cancer cell lines)

=> => fil cancer
FILE 'CANCERLIT' ENTERED AT 12:07:40 ON 01 SEP 2004

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L33 ANSWER 1 OF 1 CANCERLIT on STN
AN **2002163411** CANCERLIT
DN **22062819** PubMed ID: **12068000**
TI **Insulin-like growth factor binding protein-3** inhibits the growth of non-small cell lung cancer.
AU Lee Ho-Young; Chun Kyung-Hee; Liu Bingrong; Wiehle Sandra A; Cristiano Richard J; Hong Waun Ki; Cohen Pinchas; Kurie Jonathan M
CS Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.. hlee@mdanderson.org
SO CANCER RESEARCH, **(2002 Jun 15)** 62 (12) 3530-7.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2002333234
EM 200207
ED Entered STN: 20020819
Last Updated on STN: 20020819
AB Insulin-like growth factors (IGFs) have mitogenic and antiapoptotic properties and have been implicated in the development of lung cancer. The effects of IGFs are modulated by insulin-like growth factor binding proteins (IGFBPs). This study explored the effects of **IGFBP-**

3 on non-small cell lung cancer (NSCLC) cells after infection with an adenovirus constitutively expressing **IGFBP-3** under the control of the cytomegalovirus promoter (Ad5CMV-BP3). We found that IGFs, especially IGF-I, stimulated the growth of NSCLC cells, and Ad5CMV-BP3 suppressed this IGF-I-induced NSCLC cell growth. We also found that the clonogenicity of H1299 cells in soft agar was markedly reduced by Ad5CMV-BP3. Furthermore, direct injection of Ad5CMV-BP3 into H1299 NSCLC xenografts s.c. established in athymic nude mice induced massive destruction of the tumors. Ad5CMV-BP3 did not induce detectable cytotoxicity on normal human bronchial epithelial cells, suggesting therapeutic efficacy of this virus. Ad5CMV-BP3 infection was accompanied by apoptotic cell death in vitro as detected by flow cytometry, DNA fragmentation analysis, and Western blot analysis on the expression of Bcl-2 and on the cleavage of poly(ADP-ribose) polymerase, a substrate of caspase 3. Immunofluorescence confocal microscopy was also used to show the apoptotic effect of Ad5CMV-BP3 in H1299 tumors established in nude mice. These findings indicated that **IGFBP-3** was a potent inducer of apoptosis in NSCLC cells in vitro and in vivo. To delineate the underlying mechanism, we examined the effect of **IGFBP-3** on Akt/protein kinase B and glycogen synthase kinase-3beta, downstream mediators of the phosphatidylinositol 3-kinase pathway, and on mitogen-activated protein kinase (MAPK), all three of which are activated by IGF-mediated signaling pathways and have important roles in cell survival. **IGFBP-3** overexpression inhibited the phosphorylation of Akt and glycogen synthase kinase-3beta and the activity of MAPK. Furthermore, IGF-I rescued the NSCLC cells from serum depletion-induced apoptosis, and this rescue was blocked in Ad5CMV-BP-3-infected H1299 NSCLC cells. Transient transfection with activated Akt or constitutively active MAPK kinase-1, an upstream activator of MAPK, partially blocked **IGFBP-3**-induced apoptosis of NSCLC cells. These findings suggested that the growth-regulatory effect of **IGFBP-3** on NSCLC cells was attributable in part to the inhibition of the IGF-induced survival pathway. These data demonstrate the importance of **IGFBP-3** in the regulation of NSCLC cell proliferation, clonogenicity, and tumor growth, suggesting that **IGFBP-3** is a target for the treatment of lung cancer and that Ad5CMV-BP3 is a potential therapeutic agent.

CT Check Tags: Animal; Female; Human
1-Phosphatidylinositol 3-Kinase: AI, antagonists & inhibitors
1-Phosphatidylinositol 3-Kinase: PH, physiology
Adenoviridae: GE, genetics
Apoptosis: PH, physiology
Carcinoma, Non-Small-Cell Lung: GE, genetics
Carcinoma, Non-Small-Cell Lung: ME, metabolism
*Carcinoma, Non-Small-Cell Lung: PA, pathology
Cell Division: PH, physiology
Gene Transfer Techniques
Insulin-Like Growth Factor Binding Protein 3: BI, biosynthesis
Insulin-Like Growth Factor Binding Protein 3: GE, genetics
***Insulin-Like Growth Factor Binding Protein 3: PH, physiology**
Lung Neoplasms: GE, genetics
Lung Neoplasms: ME, metabolism
***Lung Neoplasms: PA, pathology**
MAP Kinase Signaling System: PH, physiology
Mice
Mice, Nude
Mitogen-Activated Protein Kinase Kinases: BI, biosynthesis
Mitogen-Activated Protein Kinase Kinases: GE, genetics
Mitogen-Activated Protein Kinase Kinases: PH, physiology
Protein-Serine-Threonine Kinases: BI, biosynthesis
Protein-Serine-Threonine Kinases: GE, genetics
Protein-Serine-Threonine Kinases: PH, physiology

Proto-Oncogene Proteins: AI, antagonists & inhibitors
Proto-Oncogene Proteins: PH, physiology

CN **0 (Insulin-Like Growth Factor Binding Protein 3)**; 0 (MAP Kinase Signaling System); 0 (Proto-Oncogene Proteins); 0 (proto-oncogene protein akt); EC 2.7.1.- (MEK1 protein); EC 2.7.1.- (Protein-Serine-Threonine Kinases); EC 2.7.1.137 (1-Phosphatidylinositol 3-Kinase); EC 2.7.10.- (Mitogen-Activated Protein Kinase Kinases)

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